FABRICATION 2
LECTURE 6

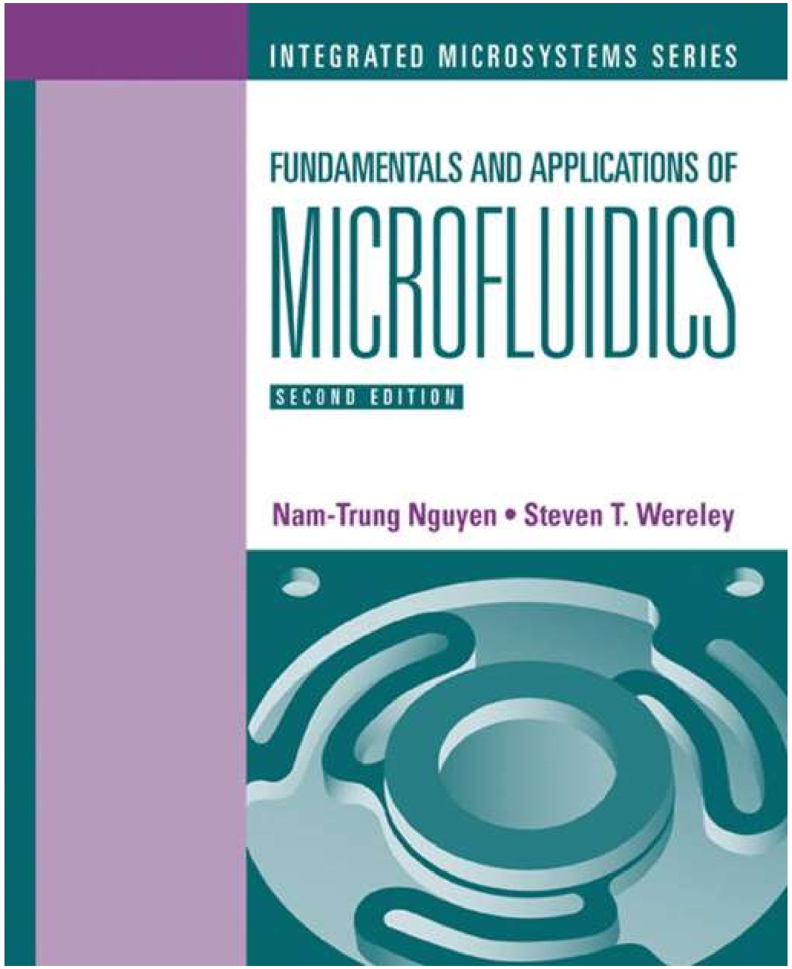
Tamás Pardy
TalTech Lab-on-a-Chip

13.01.2022

TALLINN UNIVERSITY OF TECHNOLOGY

BEFORE WE BEGIN…

- Fundamentals and Applications of Microfluidics (2nd edition) – **Chapter III**
- Nam-Trung Nguyen, Steven T. Wereley
- ISBN-10 1-58053-972-6
  ISBN-13 978-1-58053-972-2



OVERVIEW

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INDUSTRIAL FABRICATION

- Hot embossing
- Injection molding

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INTRODUCTION: MICROFLUIDIC SETUPS

1. Traditional flow chemistry setup
    - Professional analytical laboratories, including medical diagnostics (**chip in a lab**)
    - Target: lower cost OR better volume control
    - Expensive instrumentation but cheap assay

2. **Cartridge + reader**
    - Point-of-Care/Point-of-Need analytics
    - Target: wider availability
    - Mid-range instrumentation cost, mid-range assay cost

3. Fully integrated (true **lab-on-a-chip**)
    - Homecare diagnostics
    - Target: home & office diagnostics
    - Low instrument cost, high assay cost

1.

2.

3.

https://syrris.com/product/asia-flow-chemistry/
http://clinchem.aaccjnls.org/content/59/4/629
www.medicalexpo.com/prod/selfdiagnostics-deutschland-gmbh/product-121137-843335.html

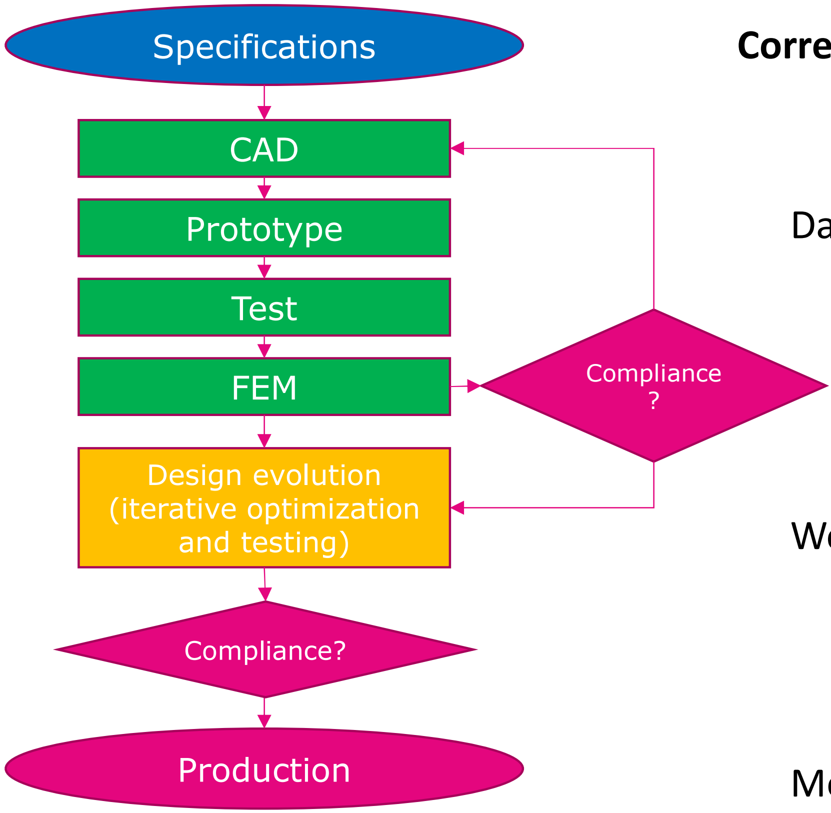
COMPUTER-AIDED ENGINEERING

Specifications

Feasibility

Concept

Production



Correcting an error…

Days & €100-1000

Weeks… & €1000-10000

Months… & >€10000

http://web.mit.edu/16.810/www/16.810_L4_CAE.pdf

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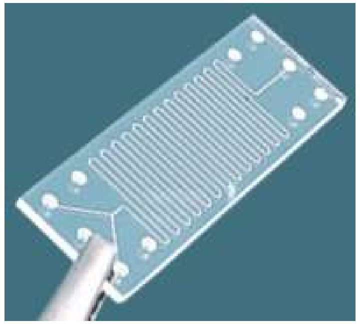
Speaking from experience here…

FABRICATION TECHNIQUES FOR POLYMERS

- Why polymers?
  - **Cheap (max. 1-2 EUR per chip)**
  - Easy to machine
  - Optically transparent (if needed)
  - Good thermal and electrical properties
  - High aspect-ratio for microstructures
  - Biocompatible (if needed)
  - Recyclable options available

- **Plastics are particularly well-suited for single-use rapid tests (e.g. pregnancy test)**

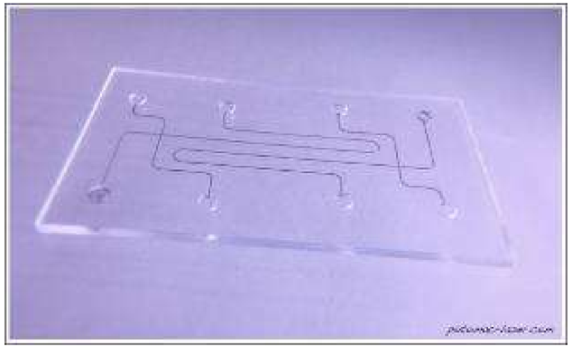


https://syntecoptics.com/polymer-optics-microfluidics/polymer-microfluidic-devices

https://en.wikipedia.org/wiki/HCG_pregnancy_strip_test

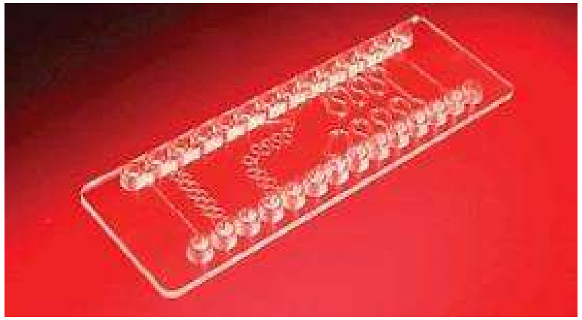
FABRICATION TECHNIQUES FOR POLYMERS

- PMMA (Polymethyl methacrylate)
  - Transparent thermoplastic
  - Chemically resistant, mechanically robust
  - Good for hot embossing (see later) and milling



Property	Value
ε	4.9
Melting point	160 °C
k	0.18 W/(mK)
ρ	2e15 Ωcm

- COC (Cyclic olefin copolymer)
  - Chemically resistant, mechanically robust
  - Good for injection moulding (see later)



Property	Value
ε	2.35
Melting point	75-170 °C
k	0.12-0.15 W/(mK)
ρ	1e15Ωm

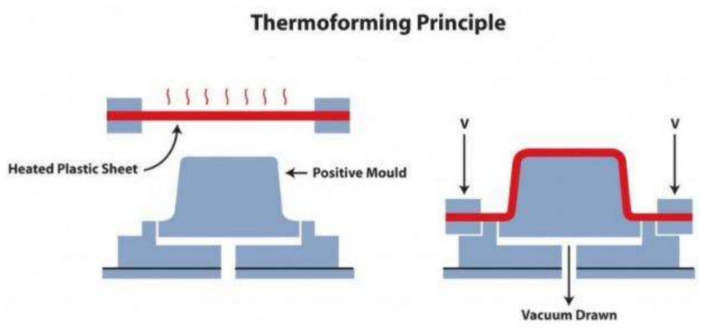
FABRICATION TECHNIQUES: HOT EMBOSSING

- **Hot embossing (microthermoforming)**
  process of forming heated plastic sheets to a specific shape using a mould.

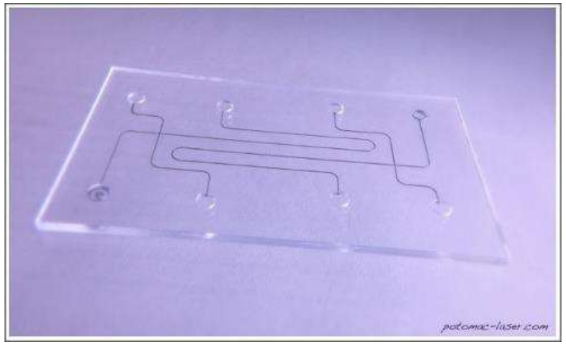
- **Animation**: link
  Video: https://youtu.be/GcWD9AP6f8U?t=32

- **Input**: patterned positive master mould
  Output: patterned plastic sheet/ polymer layer

- **Thermoplastic nanoimprint lithography (T-NIL)**
  hot embossing in nanoscale, but instead of a plastic sheet, a thermoplastic polymer layer is imprinted.



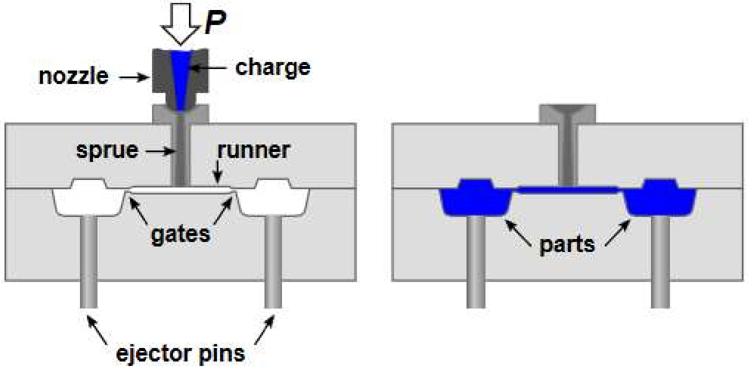
http://www.euroextrusions.com/the-principle-of-thermoforming/



http://www.potomac-laser.com/wp-content/uploads/2015/05/MF_ink.jpg

FABRICATION TECHNIQUES: INJECTION MOULDING

- **Injection moulding:**
  - process by which material is formed by injection into a mould. The material is fed into the mould cavity through a heated barrel at high pressure.
- **Video**: https://youtu.be/b1U9W4iNDiQ?t=22
- **The mould is machined from metal**
  - Steel for mass production (>1 M)
  - Aluminium for small-series production (10k)
- **Not suitable for prototyping!**
  - **Injection moulding is not suitable for prototyping! A mould typically costs on the order of 100kEUR, so any design change is ill-advised.**
- **Input**: machined metal mould
  Output: injection moulded plastic part



https://en.wikipedia.org/wiki/Injection_moulding

https://cdn.technologyreview.com/i/legacy/sia_x600.jpg

FABRICATION TECHNIQUES: COMPARISON

	Milling	Hot embossing	Injection moulding
Mould cost	0	$ or $$	€10-100k
Cost/pc (mass-production)	€10-100	$$	€<1
Best applied for	Prototyping	Prototyping and production	Production only
Typical chip layer structure	Multilayer	Multilayer	Monolithic
Minimum feature size	2.5-7.5 µm	<100 nm (via NIL)	50-100 nm

INDUSTRIAL FABRICATION

- Hot embossing
- Injection molding

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MICROFABRICATION

- Clean rooms
- Materials

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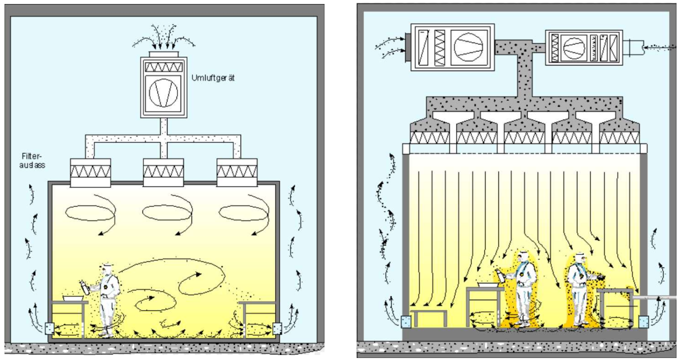
1. INTRODUCTION: CLEAN ROOM

Clean room = facility utilized as part of specialized industrial production or scientific research, including the manufacture of pharmaceutical items and microprocessors

Clean room air has low levels of particulates (standard: ISO 14644-1)

Turbulent Laminar



https://en.wikipedia.org/wiki/Cleanroom#/media/File:Laminar_Flow_Reinraum.png

Class	Maximum particles/m^3 [a]						FED STD 209E equivalent
	≥0.1 µm	≥0.2 µm	≥0.3 µm	≥0.5 µm	≥1 µm	≥5 µm	
ISO 1	10 [b]	[d]	[d]	[d]	[d]	[e]	
ISO 2	100	24 [b]	10 [b]	[d]	[d]	[e]	
ISO 3	1,000	237	102	35 [b]	[d]	[e]	Class 1
ISO 4	10,000	2,370	1,020	352	83 [b]	[e]	Class 10
ISO 5	100,000	23,700	10,200	3,520	832	[d,e,f]	Class 100
ISO 6	1,000,000	237,000	102,000	35,200	8,320	293	Class 1,000
ISO 7	[c]	[c]	[c]	352,000	83,200	2,930	Class 10,000
ISO 8	[c]	[c]	[c]	3,520,000	832,000	29,300	Class 100,000
ISO 9	[c]	[c]	[c]	35,200,000	8,320,000	293,000	Room air

[a] All concentrations in the table are cumulative, e.g. for ISO Class 5, the 10 200 particles shown at 0,3 µm include all particles equal to and greater than this size.

[b] These concentrations will lead to large air sample volumes for classification. Sequential sampling procedure may be applied; see Annex D.

[c] Concentration limits are not applicable in this region of the table due to very high particle concentration.

[d] Sampling and statistical limitations for particles in low concentrations make classification inappropriate.

[e] Sample collection limitations for both particles in low concentrations and sizes greater than 1 µm make classification at this particle size inappropriate, due to potential particle losses in the sampling system.

[f] In order to specify this particle size in association with ISO Class 5, the macroparticle descriptor M may be adapted and used in conjunction with at least one other particle size. (See C.7.)

https://en.wikipedia.org/wiki/Cleanroom

Clean room air is kept clean by continuously recirculating and filtering air in the room through HEPA or ULPA filters.

In laminar flow layouts, air comes from the ceiling and is recirculated through floor vents, taking away any particulates in the process.

1. INTRODUCTION: CLEAN ROOM

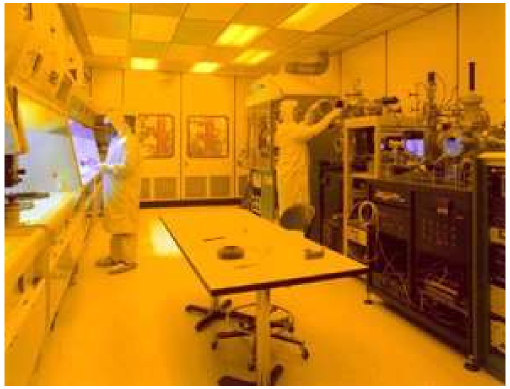
https://www.terrauniversal.com/cleanrooms/cleanroom-airlock.php

See the metal mesh? That's for **antistatic protection**.

Entry is usually through an **airlock with an air shower** stage

Protective clothing (face mask, gloves, shoes, coat) must be worn inside.

https://en.wikipedia.org/wiki/File:Cleanroom_Garment2.JPG



https://en.wikipedia.org/wiki/File:Cleanroom_outside.jpg

Yellow light prevents unwanted exposure of **photosensitive** polymers.

1. INTRODUCTION: CLEAN ROOM

- **Clean rooms are expensive:**
  - It's all pretty cool but it's hellishly expensive, right? Right, unfortunately… $1-10k/m^2
  - We don't have a clean room at TJS ELIN yet. A cheaper alternative, which is just as good but smaller: **glovebox**

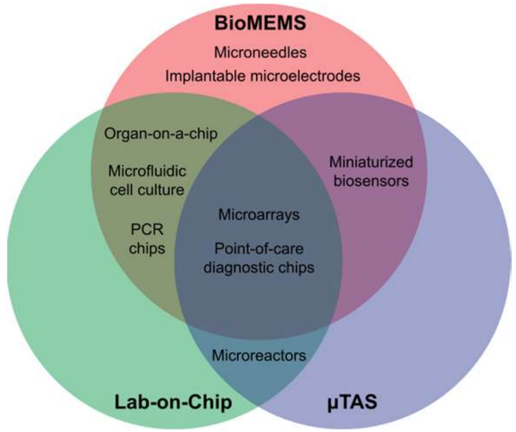
- **Gloveboxes are more accessible:**
  - sealed container designed to allow manipulation of objects in a separate atmosphere.
  - Usually an inert gas such as nitrogen or argon is used to fill the glove box at positive pressure.
  - Pressure is maintained during work and in case of leaks, the positive pressure keeps contaminants out.
  - Good enough for Lab-on-a-Chip, costs 5-20k€ used.

https://www.cysi.wang/glove-box/800.html

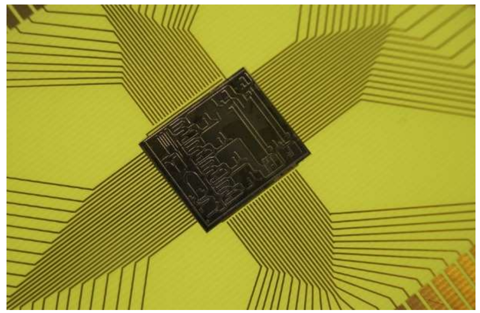
https://en.wikipedia.org/wiki/Glovebox

1. INTRODUCTION: MICROFABRICATION

- **Microfabrication**: process for the production of devices in the submicron to millimeter range.
- **MEMS** (Microelectromechanical systems): microscopic devices, esp. with moving parts. Components in range 1-100 µm, device in range 20 µm – 1 mm.
- **BioMEMS:** biomedical MEMS.
- **µTAS**=micro total analysis system
- **Lab-on-a-Chip**
  - it all started in a clean room in 1979 (S.C. Terry, Stanford University) with a gas chromatograph…
  - (analytical chemistry drove LoC for a long time, then it turned towards diagnostics)



https://en.wikipedia.org/wiki/Bio-MEMS



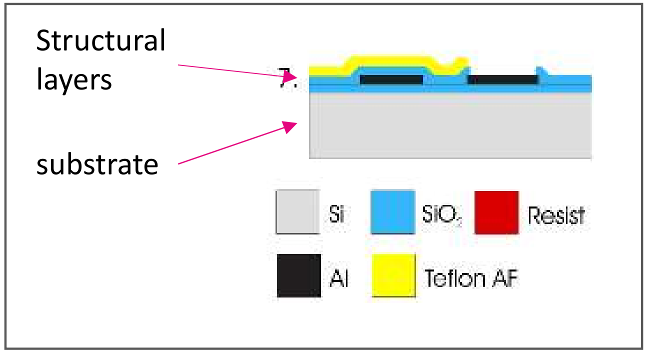
https://en.wikipedia.org/wiki/File:Labonachip20017-300.jpg

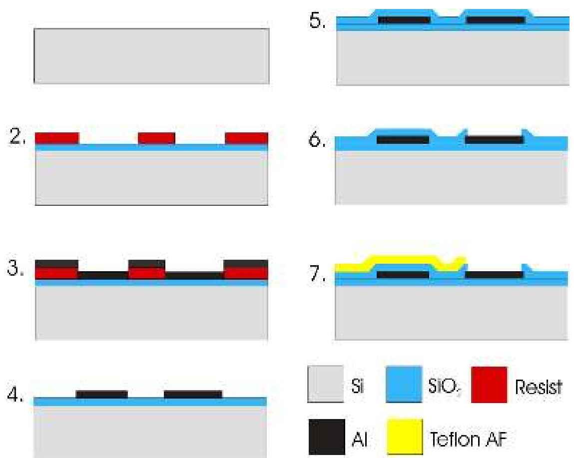
https://en.wikipedia.org/wiki/Microelectromechanical_systems
*James B. Angell; Stephen C. Terry; Phillip W. Barth (April 1983). "Silicon Micromechanical Devices". Scientific American. **248** (4): 44–55. doi:10.1038/scientificamerican0483-44.*

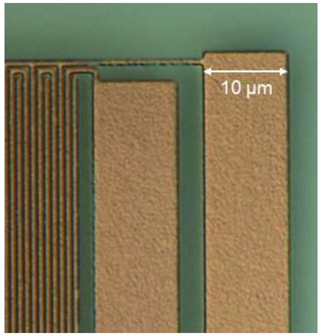
1. INTRODUCTION: MICROFABRICATION

- **Substrate**: the physical material upon which the device is built (*~underlayer)*
- **Thin film:** few nanometer to micrometer thick material layer

- Example for microfabrication process steps:

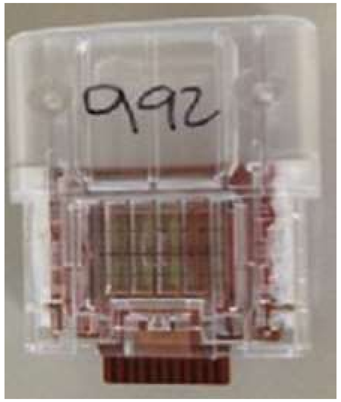






1. INTRODUCTION: MICROFABRICATION

- **Pros:**
  - Microfabrication yields structures with high aspect ratios
  - Good for feature sizes under 100 µm, ideal under 10 µm
  - Wide material selection, high production quality and good process control
  - Integration of electronics in the chip
  - Cheap in large quantities
- **Cons:**
  - Very expensive to prototype and upscale
  - Is ‘clean industry’ but uses hazardous chemicals and gases
  - Instrumentation is hellishly expensive (>1M€ to set up a clean room with some instrumentation)

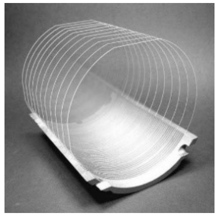


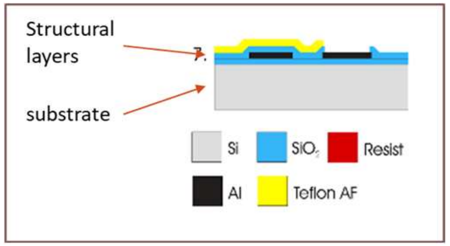
https://www.nature.com/articles/srep36000/figures/1

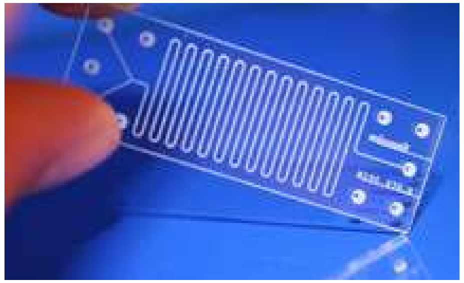
This level of integration is only possible via microfabrication but the barrier to entry is too high for startups

2. SUBSTRATES AND STRUCTURAL MATERIALS

- Substrate options







	Silicon	Glass
Pros	Resistant to organic solvents, good thermal conductivity	Chemically resistant, transparent
Cons	Expensive, not transparent	Expensive, permeable to gas

Typically silicon-silicon or glass-glass chips

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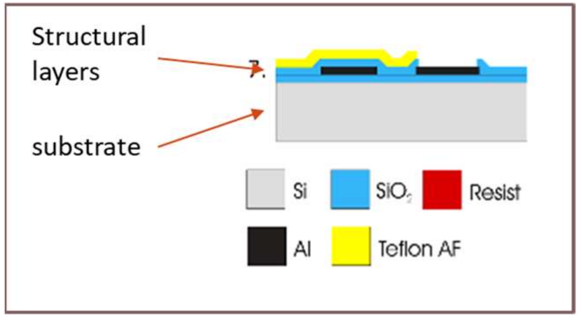
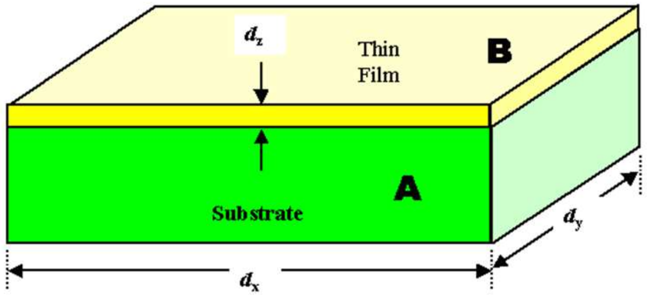
https://www.elveflow.com/microfluidic-tutorials/microfluidic-reviews-and-tutorials/materials-for-microfluidic-chips-fabrication-a-review-2017/
https://www.indiamart.com/proddetail/n-type-silicon-wafer-10259007573.html
https://www.indiamart.com/proddetail/glass-wafers-5045832862.html

2. SUBSTRATES AND STRUCTURAL MATERIALS

- **Structural materials are typically deposited as thin films**
- **Most commonly used thin films are:**
  - Silicon dioxide (SiO_2)
    - Thermal oxide or CVD oxide (we'll talk about these later)
    - Electrical insulation, mask, sacrificial layer
  - Silicon Nitride (Si_3N_4)
    - Electrical insulation between conductive layers
    - Highly selective etching
    - Structural support
  - Metal films (e.g. aluminum, gold, platinum)
    - Conductive tracks, electrodes etc.
    - Aluminum used as optically reflective layer
  - Transparent conducting films (TCF)
    - Indium tin oxide (ITO)
    - Carbon nanotube





https://www.tf.uni-kiel.de/matwis/amat/semitech_en/kap_3/backbone/r3_2_2.html

MICROFABRICATION

- Clean rooms
- Materials

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MICROFABRICATION PROCESSES

- Additive processes
- Subtractive processes
- Photolithography and lift-off
- Soft lithography

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3. MICROFABRICATION PROCESSES

Additive processes	Subtractive processes
3D printing Jet printing (e.g. FDM) Selective photopolymerization (SLA, DLP) Selective sintering (SLS)	**Surface micromachining** thin films are deposited **on the substrate** and micromachined (e.g. lift- off process)
Layer deposition Mostly thin film deposition Vapor phase deposition (PVD, CVD) Liquid phase deposition (spin coating)	**Bulk micromachining**: the bulk of the **substrate** is micromachined

3. ADDITIVE PROCESSES

- Physical deposition (vapor-phase):
  - Thermal oxidation
  - Evaporation
  - Sputtering
  - Arc vapor deposition
  - Laser ablation
  - Ion plating
- Liquid phase deposition
  - Spin coating or dip coating
  - Chemical vapor deposition (CVD)
    - Plasma enhanced CVD
    - Atmospheric pressure CVD
    - Low-Pressure CVD
- Epitaxy

This is the arsenal, but we only focus on the ones most relevant to BioMEMS

3. ADDITIVE PROCESSES

- **Physical deposition (vapor-phase):**
  - **Thermal oxidation**
  - **Evaporation**
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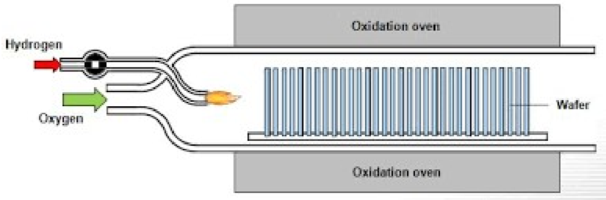
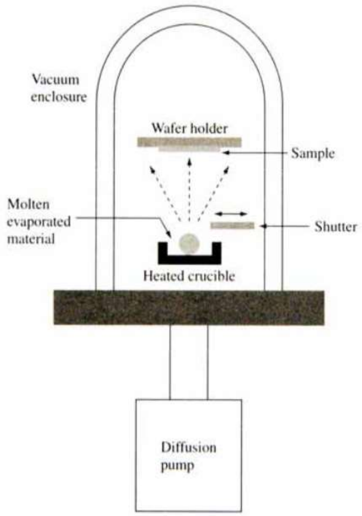
High Temperature Oxide layer (HTO) 800-1200 °C
With water/oxygen with/without HCl



http://lnf-wiki.eecs.umich.edu/wiki/File:Thermal.png



Gardner JW et al, Microsensors, MEMS and Smart Devices, 2001

Evaporation of source material in vacuum

3. ADDITIVE PROCESSES

- Physical deposition (vapor-phase):
  - Thermal oxidation
  - Evaporation
  - **Sputtering (deposition)**
  - Arc vapor deposition
  - Laser ablation
  - Ion plating
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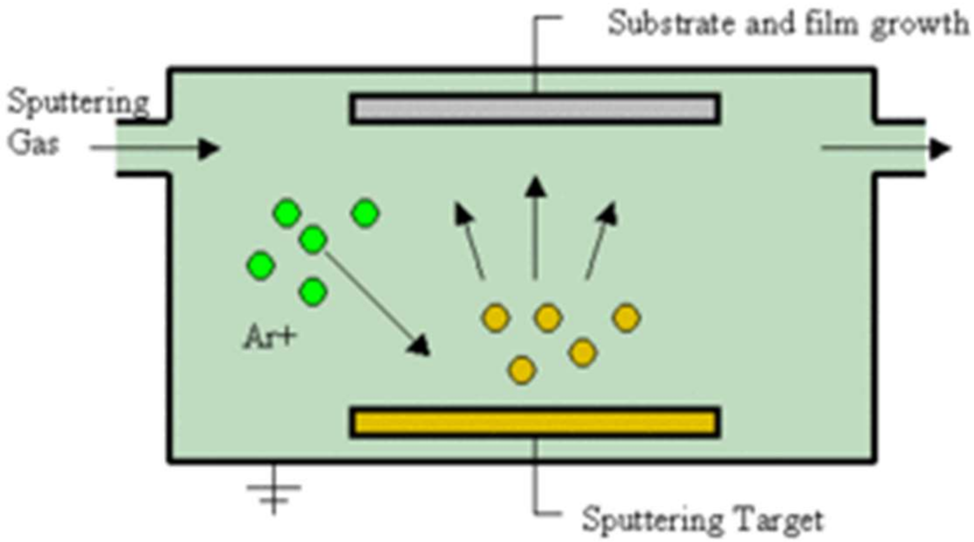

Sputtering = ejection of microparticles from surface of a solid upon bombardment with high-energy plasma/gas

(Re-)sputtering: physical vapor deposition in plasma
Sputtering gas = Inert gas plasma
Eroding from target ➔ depositing on substrate

3. ADDITIVE PROCESSES

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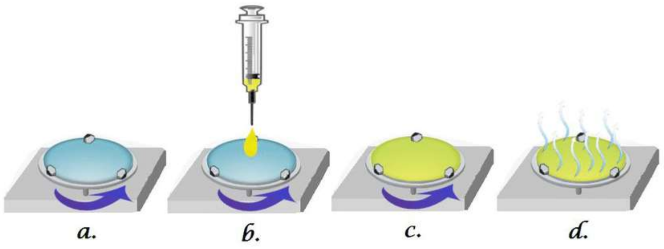

https://www.researchgate.net/figure/Spin-coating-process-of-polyamide-6-thin-films_fig3_311616041

We have a POLOS SPIN150i

- Wafer size 5-450 mm
- Speed 1-12k RPM

https://www.spincoating.com/

3. ADDITIVE PROCESSES

- Physical deposition (vapor-phase):
  - Thermal oxidation
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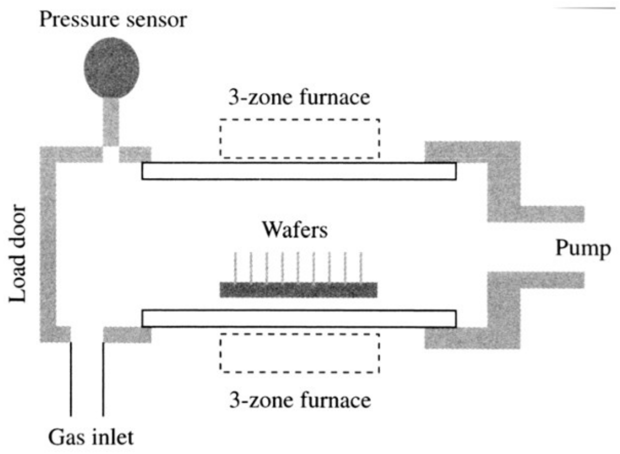

Typically, CVD done in vacuum. Produces high-quality thin films

Gardner JW et al, Microsensors, MEMS and Smart Devices, 2004

https://en.wikipedia.org/wiki/Chemical_vapor_deposition

3. SUBTRACTIVE PROCESSES

- Dry etching (plasma):
  - Glow discharge methods (diode setups):
    - Plasma etching (PE),
    - Reactive ion etching (RIE),
  - Ion beam methods (triode setups):
    - Ion beam milling (IBM),
    - Reactive ion beam etching (RIBE),
    - Chemical assisted ion beam etching (CAIBE).
  - Deep Reactive Ion Etching (DRIE).
- Wet etching (chemical liquids).

This is the arsenal, but we only focus on the ones most relevant to BioMEMS

https://en.wikipedia.org/wiki/Reactive-ion_etching#/media/File:Rieoperation.svg

3. SUBTRACTIVE PROCESSES

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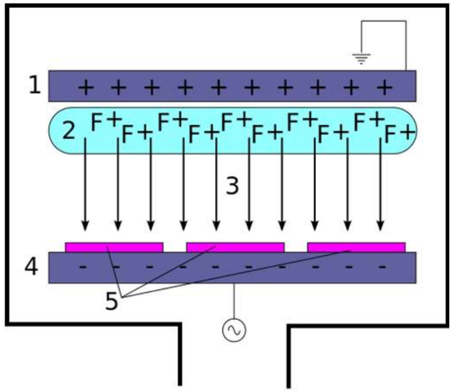
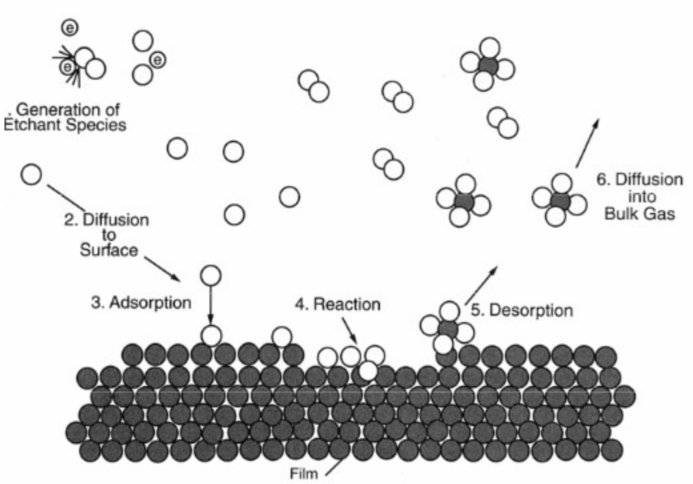


RIE: Electrodes 1), 4) create electric field 3), accelerating ions 2) toward sample surface 5)



Madou M, Fundamentals of Microfabrication, 2002

https://en.wikipedia.org/wiki/Reactive-ion_etching#/media/File:Rieoperation.svg

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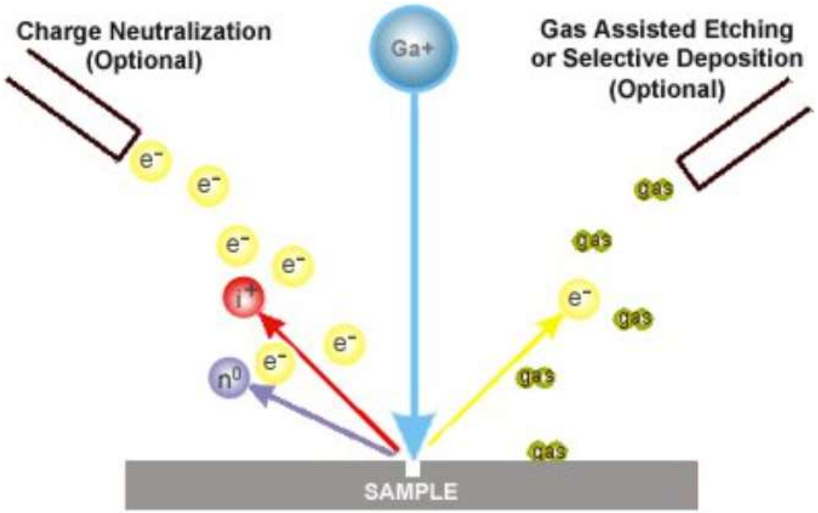
  - Deep Reactive Ion Etching (DRIE).
- Wet etching (chemical liquids).



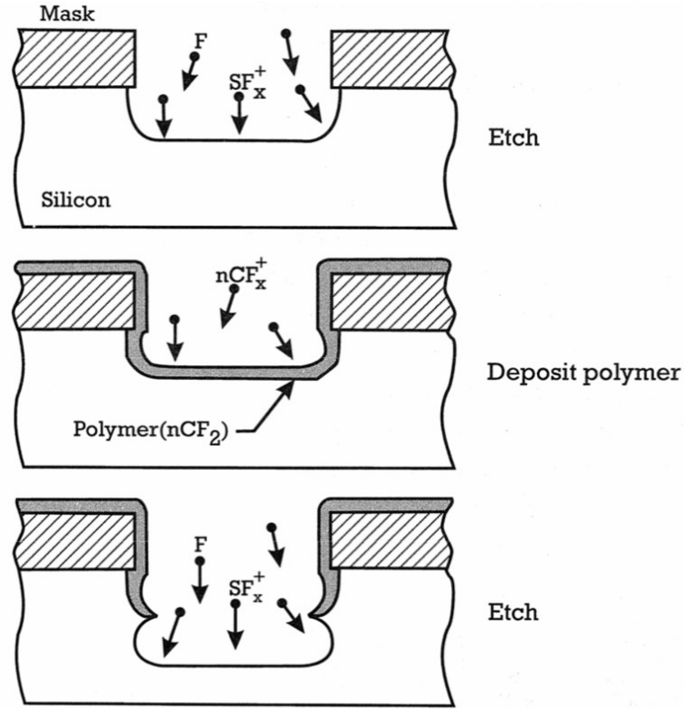
https://en.wikipedia.org/wiki/Focused_ion_beam

Focused stream of ions, e.g. gallium
Sputtering/milling

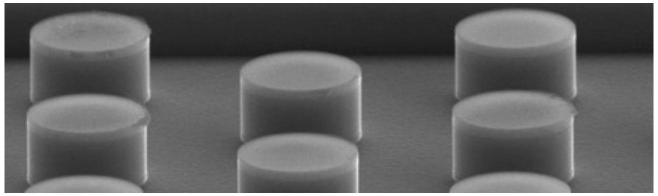
Madou M, Fundamentals of Microfabrication, 2002

3. SUBTRACTIVE PROCESSES

- Dry etching (plasma):
  - Glow discharge methods (diode setups):
    - Plasma etching (PE),
    - Reactive ion etching (RIE),
  - Ion beam methods (triode setups):
    - Ion beam milling (IBM),
    - Reactive ion beam etching (RIBE),
    - Chemical assisted ion beam etching (CAIBE).
  - **Deep Reactive Ion Etching (DRIE).**
- Wet etching (chemical liquids).



https://www.micronit.de/technologies/dry-etching-drie/

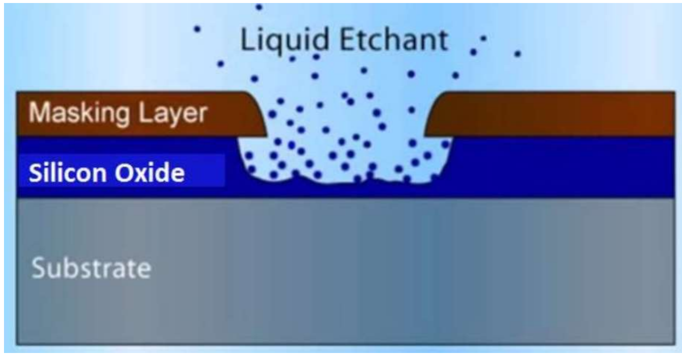


Source: Maluf 2005

3. MICROFABRICATION PROCESSES

- Dry etching (plasma):
  - Glow discharge methods (diode setups):
    - Plasma etching (PE),
    - Reactive ion etching (RIE),
  - Ion beam methods (triode setups):
    - Ion beam milling (IBM),
    - Reactive ion beam etching (RIBE),
    - Chemical assisted ion beam etching (CAIBE).
  - Deep Reactive Ion Etching (DRIE).
- **Wet etching (chemical liquids).**

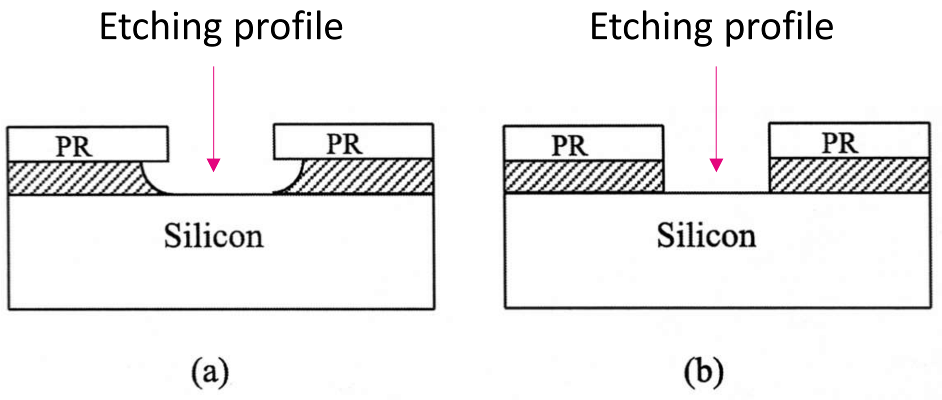
ALWAYS USE PROTECTIVE CLOTHING AND OBSERVE SAFETY INSTRUCTIONS!



Done using aggressive chemicals, e.g. NaOH, KOH, HF, BF_6, BCL_3

https://www.slideshare.net/deepak10rawat/etching-55985755
https://en.wikipedia.org/wiki/Corrosive_substance

3. MICROFABRICATION PROCESSES



Isotropic Etching

Anisotropic Etching

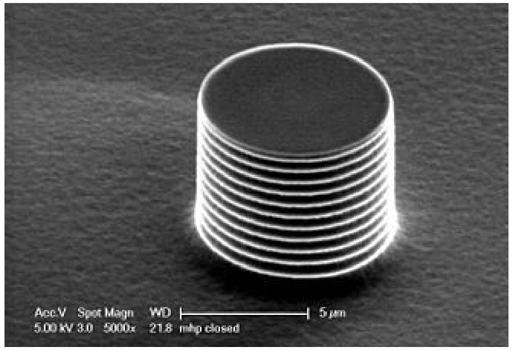
Wet etching typically has isotropic etching profiles

DRIE is highly anisotropic, but only achieves this via cyclic passivation

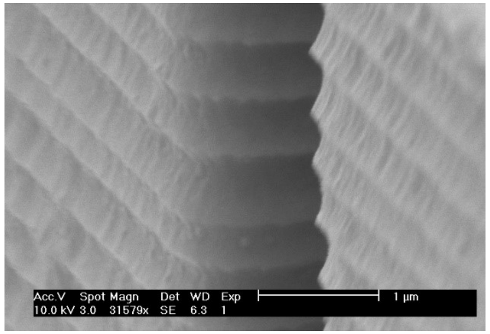
Source: Steven S. Saliterman, MD, FACP. Ziaie B et al, Hard and Soft Micromachining for BioMEMS, 2004.

3. MICROFABRICATION PROCESSES

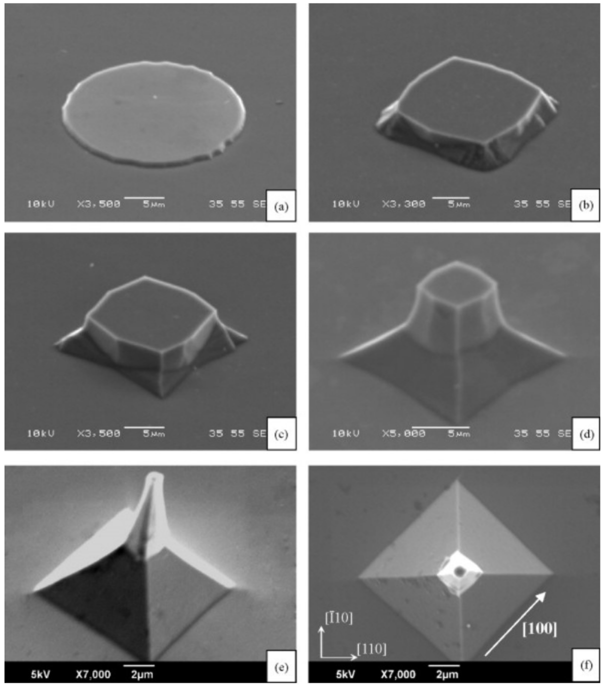
DRIE



https://en.wikipedia.org/wiki/Deep_reactive-ion_etching



Anisotropic wet etching



https://www.sciencedirect.com/science/article/pii/S0924424709001526#fig3

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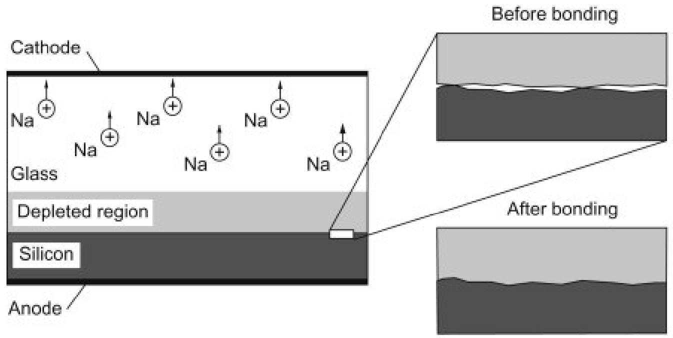
3. MICROFABRICATION PROCESSES

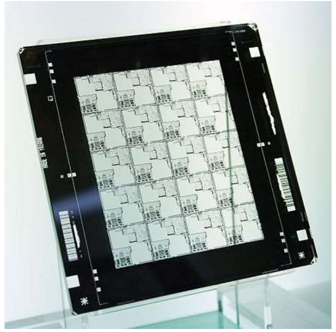
- **Chip bonding**:
  - you need to bond the two halves of the chip together to seal it
- **Direct bonding:**
  - Anodic bonding of silicon to glass
  - Silicon direct bonding
- **Intermediate adhesive layers**
  - Thermoplastics
  - Solvents
  - Double-sided tape ☺
- **Welding**
  - Laser welding
  - Ultrasonic welding
  - Diffusion welding

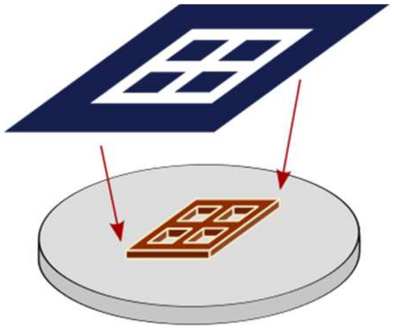


https://www.sciencedirect.com/science/article/pii/B9780323299657000300

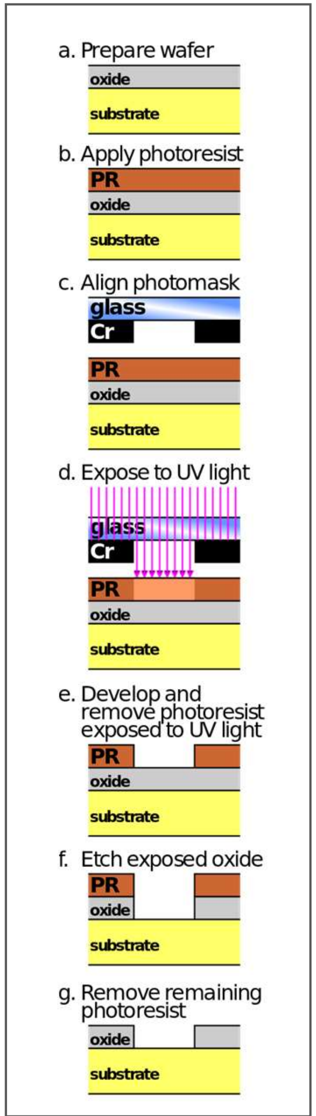
3. MICROFABRICATION PROCESSES

- **Photolithography:**
  - Used for selective etching of oxide layers
  - Needs a photomask
  - Positive photoresist: soluble where exposed
  - Negative photoresist: insoluble where exposed
- **Process:**
  a. Cleaning and preparation of wafer
  b. Application of photoresist by spin coating and prebaking at 90-100 °C, 30-60 s
  c. Mask alignment
  d. Exposure to UV light
  e. Post-exposure bake at 120-180 °C, 20-30 min and then develop. Wash away soluble resist.
  f. Etch exposed oxide (wet or dry)
  g. Remove resist residue.





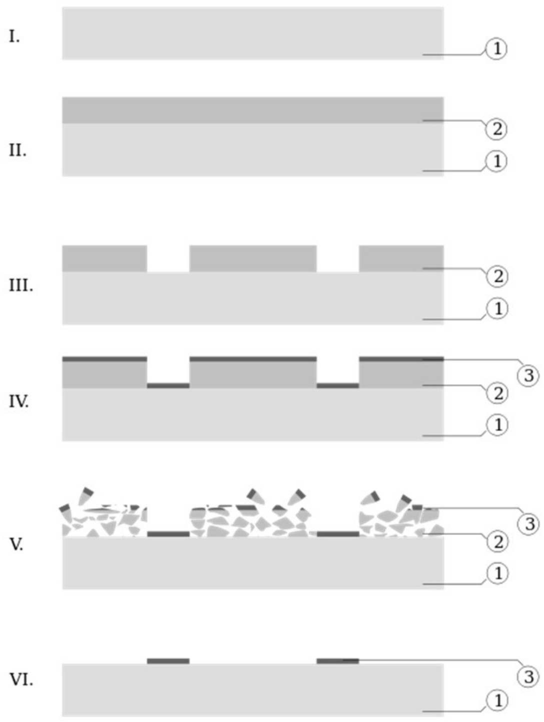
https://en.wikipedia.org/wiki/Photolithography#/media/File:Photolithography_etching_process.svg



https://en.wikipedia.org/wiki/Photomask

3. MICROFABRICATION PROCESSES

- **Photolithography and lift-off process**
  1. Preparation of the substrate
  2. Deposition of the sacrificial stencil layer
  3. Patterning the sacrificial layer (ex. etching), creating an inverse pattern
  4. Deposition of the target material
  5. Washing out the sacrificial layer together with the target material on its surface
- **Pattern Layers:**
  1. Substrate
  2. Sacrificial layer
  3. Target material
- **Mostly used to create metallic interconnections.**

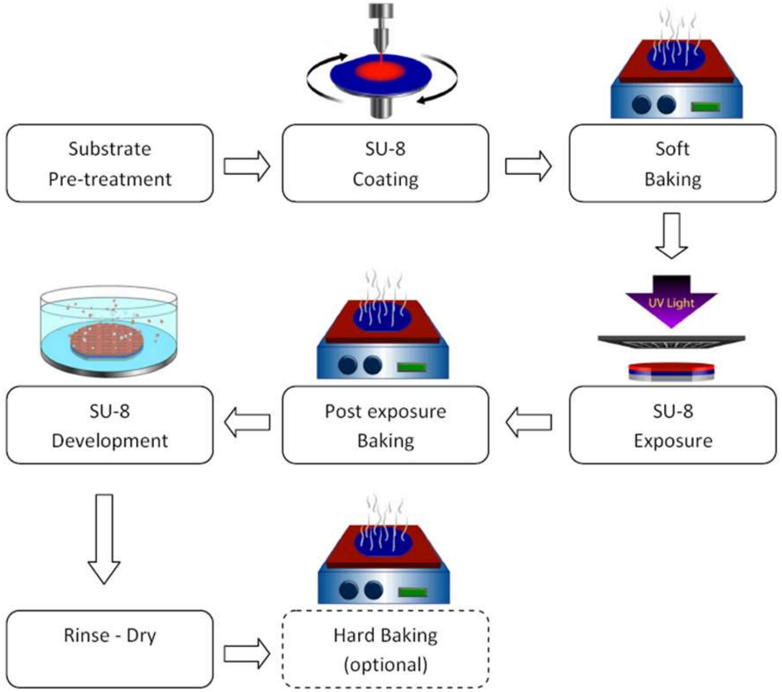


By Twisp - Own work, Public Domain,
https://commons.wikimedia.org/w/index.php?curid=3841773

https://en.wikipedia.org/wiki/Lift-off_(microtechnology)

4. MICROFABRICATION OF LAB-ON-A-CHIP DEVICES

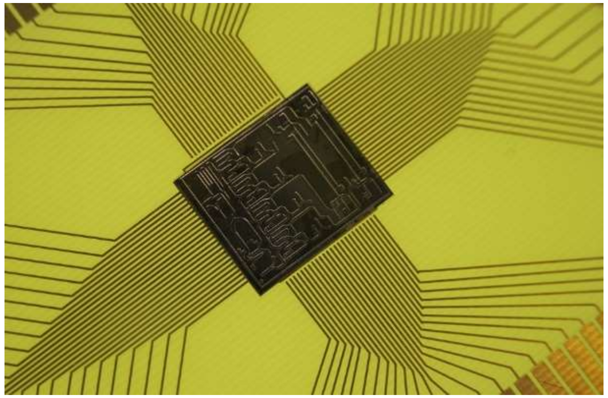
- **SU8 soft lithography**
  - negative
  - thick resist (thickness up to 0.5 mm or even 1 mm)
  - can be used for molding PDMS
- **Advantages: cheaper instrumentation**
  - Clean room not needed
  - Reasonable instrumentation cost (50-100k€)
  - Minimally spin coater, hot plate, mask aligner or LDI system needed
  - LDI (laser direct imaging) doesn’t need a mask, uses UV laser to expose resist
  - Produces structures with good aspect ratios
- **Disadvantages: lower quality than Si masks**
  - Resolution & mold lifetime lower than with silicon molds
  - Silicon-glass or glass-glass chips are far more robust



https://www.elveflow.com/microfluidic-tutorials/soft-lithography-reviews-and-tutorials/introduction-in-soft-lithography/su-8-mold-lithography/

4. MICROFABRICATION OF LAB-ON-A-CHIP DEVICES

- **Silicon-glass and glass-glass chips**
- **Process**:
  - One or both sides are structured with surface and/or bulk micromachining
  - The two sides are bonded together
- **Advantages:**
  - Very high aspect ratio
  - Possibility to integrate electronics
  - Excellent process control
- **Disadvantages:**
  - Initial investment is huge
  - Only makes sense in professional market
- Both silicon and glass can be combined with hard polymers too



MICROFABRICATION PROCESSES

- Additive processes
- Subtractive processes
- Soft lithography

13.01.2022

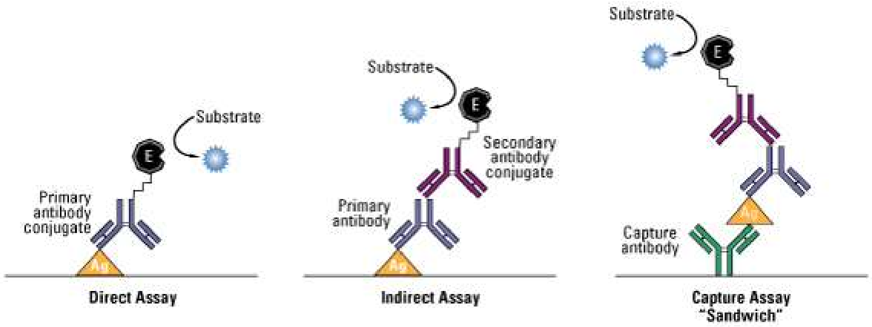
COMMERCIAL EXAMPLES

- Immunoassays
- Nucleic acid amplification tests

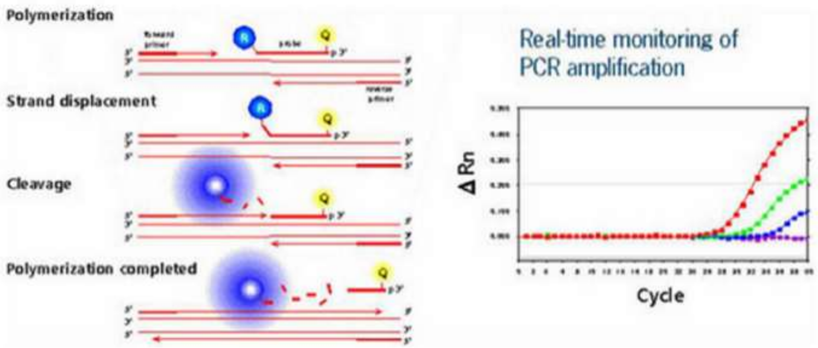
13.01.2022

IMMUNOASSAY VS. NAAT

- **Immunoassay**:
  - biochemical test that measures the presence/concentration of a molecule in a solution using an antibody/antigen.
  - Detects an already present immune response
  - This needs a few days – few weeks time!
  - **In the case of infectious diseases, the host keeps infecting during the incubation time, not knowing about their infection…**



- **Nucleic acid amplification test:**
  - a molecular technique to detect a target pathogen in a specimen, typically a body fluid, by amplifying the concentration of its DNA/RNA (bacteria/viruses)
  - **Instantaneous, extremely sensitive & specific**

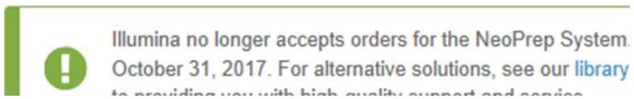


https://www.thermofisher.com/content/dam/LifeTech/global/life-sciences/protein-biology/PBLC/1499003520217.jpg
https://www.intechopen.com/source/html/49685/media/fig1.png

DMF: ILLUMINA NEOPREP

- **NeoPrep NGS Library Prep with Digital Microfluidics**
  - **Platform**: PCB two-plate DMF with filler fluid
  - **Product**: Next generation sequencing tool for DNA sequencing and library preparation
  - **Input**: various
  - **Output**: genome library
  - Now Illumina, was: Advanced Liquid Logic LLC
  - Genome library: collection of genomic DNA from a single organism
- **Links**:
  - https://youtu.be/F_Hks6OnSKM
  - https://www.illumina.com/science/technology/digital-microfluidics.html
  - https://www.illumina.com/content/dam/illumina-marketing/documents/products/brochures/brochure-neoprep.pdf

Technical challenges in DMF….

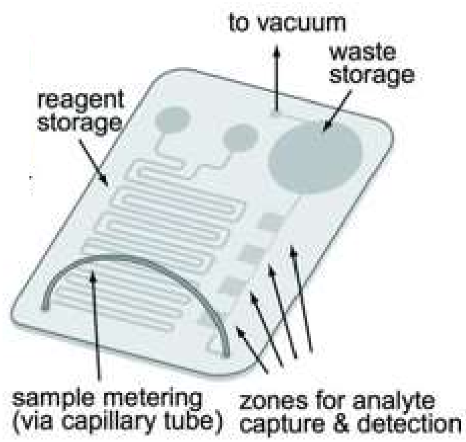


http://pubs.rsc.org/services/images/RSCpubs.ePlatform.Service.FreeContent.ImageService.svc/ImageService/Articleimage/2008/LC/b814922d/b814922d-f1.gif

MCHIP

- **System:**
  - **Platform**: Injection moulded plastic CMF chip
  - **Product**: portable HIV-1 ELISA blood test
  - **Input**: blood
  - **Output**: digitized optical readout
  - **Assay time**: 20 min

- **Functions**
  - Immunoassay test (requires 2-4 week incubation)
  - **CMF Actuation: Negative pressure driven flow**
  - Optical readout
  - Wireless data reporting (result + GPS coordinates)
  - Size: 11 cm x 7 cm x 24 cm



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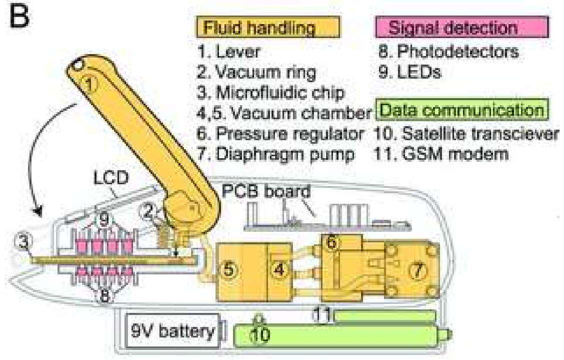

http://www.nature.com/nm/journal/v17/n8/full/nm.2408.html
https://en.wikipedia.org/wiki/MChip
https://www.youtube.com/watch?v=vpxnJM2jSVg

MCHIP

	Benchtop ELISA				Rapid test	mChip
	Liquid handling ‡	Signal detection #	Data processing & communication ^	Total	Total	Total
Space of device (in^3)	2380	2170	1170	5720	NA	180
Power of device (W)	150	300	50	500	NA	0.6
Cost of device (USD)	$9600	$8850	$1000	$19 450	NA	<$1000*
Market price per test (USD)	1.80 to 6.20				0.40 to 4.50	1.00 to 3.00**
Reagent volume/test (µL)	4400†				50 to 900	160
Sample volume/test (µL)	75†				10 to 80	0.2
Time to run assay (min)	130†				10 to 30	20
Time from sample collection to results (min)	150†				10 to 30	20
Sample throughput/day	Hundreds				Tens	Tens
Objective interpretation of results	Yes				No	Yes
Communicates with EMRs	Yes				No	Yes
Handles whole blood	No				Yes	Yes

‡ Biotek Microplate Washer ELx405 # Biotek Microplate Reader ELx808 ^Dell Latitude E6400
† Bio-Rad Genetic Systems HIV-1/HIV-2 PLUS O Enzyme Immunoassay (FDA-approved)
* estimated manufacturing cost ** estimated

When to use microfluidics (professional):

If you can make it cheaper…

Not just cheaper but…

- More widely available
- Smaller device size
- Smaller sample size (0.2 µl)
- Smaller reagent size
- Easier to use (minimal training)
- Faster detection

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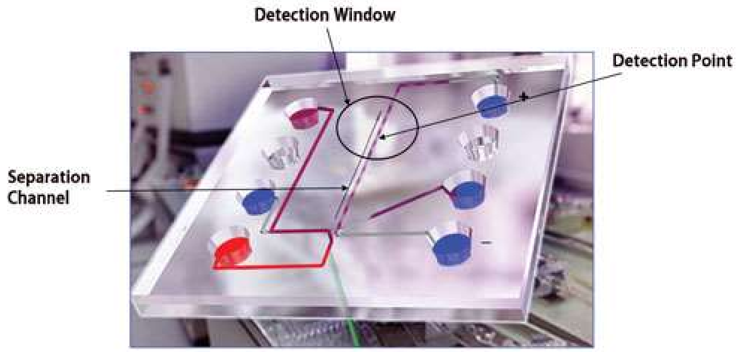
PERKINELMER LABCHIP GX TOUCH 24

- **PerkinElmer LabChip GX Touch 24**
  - **Platform**: plastic CMF chip
  - **Product**: Microfluidic capillary electrophoresis system for DNA/RNA quantification
  - **Input**: free DNA in liquid
  - **Output**: (digital) quantified DNA
  - **Assay time**: 30 seconds

- Links:
  - http://www.perkinelmer.co.uk/product/24-labchip-gx-touch-cls138162

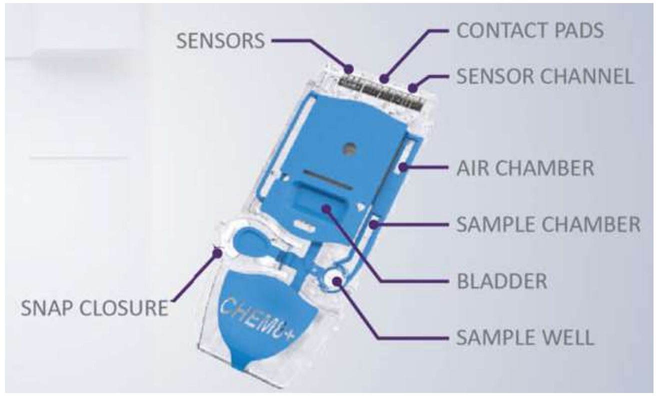


http://www.perkinelmer.co.uk/product/24-labchip-gx-touch-cls138162
https://www.genengnews.com/gen-articles/quality-assessment-of-genomic-dna-degradation/4984

ABBOTT I-STAT HANDHELD

- **i-STAT handheld**
  - **Platform**: Injection moulded CMF chips with electrochemical detector
  - **Product**: Immunoassay cartridges + handheld reader
  - **Input**: blood
  - **Output**: electrochemical readout
  - **Assay time**: 2-3 minutes

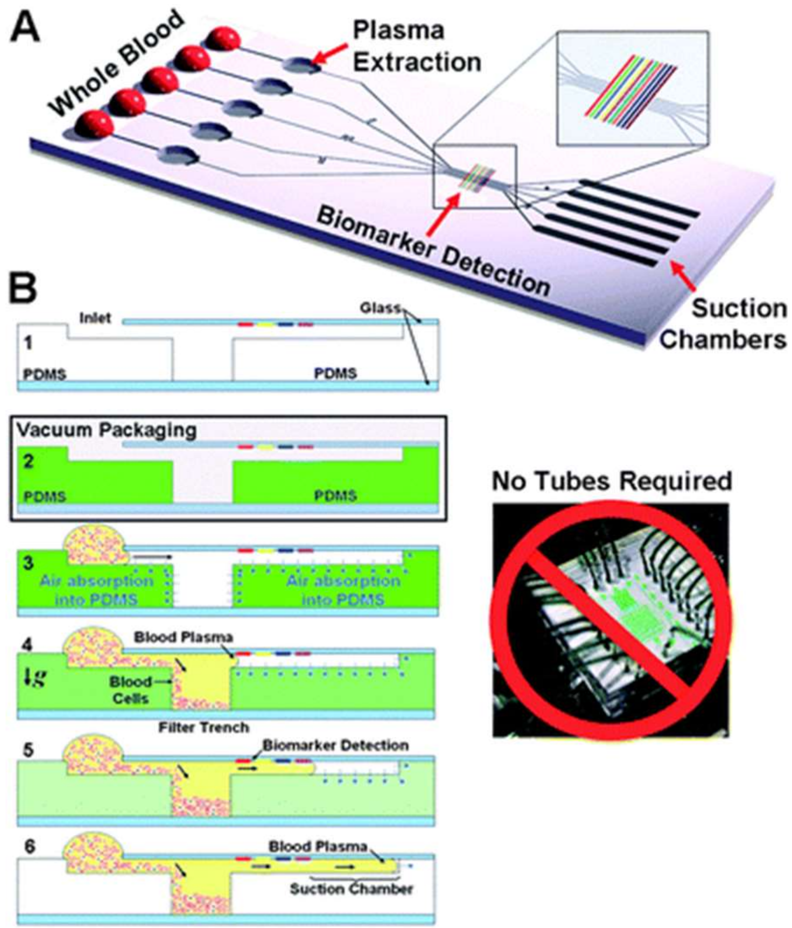
- Links:
  - https://www.pointofcare.abbott/int/en/offerings/istat/istat-handheld
  - https://www.pointofcare.abbott/download?docUri=/technical-library/static-assets/technical-documentation/4_Section 2_Testing Pro_for_iSTAT_Chem_Cart_725592-00K.pdf



https://www.pointofcare.abbott/int/en/offerings/istat/istat-handheld

SIMBAS CHIP

- **Stand-alone self-powered integrated microfluidic blood analysis system (SIMBAS)**
  - **Platform**: PDMS-glass CMF chip
  - **Product**: portable blood test
  - **Input**: 5 µl blood droplet
  - **Output**: optical readout (colorimetry)
  - **Assay time**: 10 min
- System:
  - Chip is vacuum-sealed and sucks in sample when opened
  - On-chip cell separation and plasma extraction
- Link:
  - http://pubs.rsc.org/en/content/articlehtml/2011/lc/c0lc00403k



STD MULTITEST

- **STD Multitest**
  - **Platform**: All-in-one plastic CMF chip
  - **Product**: 2nd generation RDT for the detection of sexually transmitted diseases
  - **Input**: urine
  - **Output**: lateral flow strip visualization
  - **Assay time**: 30 minutes
  - Non-instrumented nucleic acid amplification test (NINAAT) – single-use, self-contained DNA amplification platform
  - Results are on par with laboratory assays

http://selfdiagnostics.com/std-multitest/

- **Links**:
  - http://selfdiagnostics.com/std-multitest/
  - http://selfdiagnostics.com/technology/

LUCIRA CHECK-IT EASY

- **Lucira Covid-19 test kit**
  - **Platform**: All-in-one plastic CMF chip
  - **Product**: 2nd generation RDT for the detection of sexually transmitted diseases
  - **Input**: Nasal swab
  - **Output**: Colorimetry
  - **Assay time**: 11 minutes for positive result, 30 minutes for negative result
  - FDA EUA approved

- **Links**:
  - Lucira Check It COVID-19 All-In-One Test Kit – LUCIRA (lucirahealth.com)
  - Lucira COVID-19 Test Kit Demonstration - YouTube

COMMERCIAL EXAMPLES

- Immunoassays
- Nucleic acid amplification tests

13.01.2022

IEE1860 BIOMEMS

Contact: tamas.pardy@taltech.ee

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BIOMEMS

self diagnostics

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